MINIATURIZED MICROTITER PLATE FOR HIGH THROUGHPUT SCREENING

The invention relates to a miniaturized microtiter plate for HT screening (high throughput screening).

In this screening it is desirable to minimize the consumption of assay components and of the substances from the screening libraries and to maximize the throughput of screening assays. This can be achieved by miniaturizing screening assays. However, it is necessary in this case to charge appropriate microtiter plates having an assay volume of about 0.5 to 10 µl, preferably 1 to 6 µl, particularly preferably 1 to 2 µl. The only ones available to date are a few prototypes which can be processed only by particular analyzers. However, there is a need for microtiter plates which permit analysis with very sensitive detectors (with confocal optics) and allow charging with "nanodispensers". A further desirable feature is prevention of evaporation.

Microtiter plates have been disclosed by Greiner, 64943 Hirschberg, (Micro-Assay Plate, 1536 wells). In this case, the effective volume of the sample carriers is relatively large (4-8 µl) and they do not permit "single molecule detection". Although the effective volume of the Corning Costar microtiter plates (Corning Costar Deutschland, 55924 Bodenheim) is between 1 and 2 µl, the frame of the microtiter plates is too thin so that conventional robotic systems are unable to transport the microtiter plates. "Single molecule detection" is impossible in this case, too. A Hellma brochure (1994) "Silica Glass Microassay Plates" discloses microassay plates with a base made of silica glass and 384 wells with a diameter of 3.5 mm. However, besides the large assay volume, these microassay plates have frames which are insufficiently broad and bases which are too thick (> 1 mm) to allow analysis using confocal optics. US 5,487,872 describes multiassay microtiter plates for UV spectroscopy having glass plates with a minimum thickness of 0.38 mm. These microtiter plates are also unsuitable for analysis using confocal optics. Microassay plates with lids to prevent evaporation are described in a Radleys brochure (1997) "Specialist Micro Titer Plates & Accessories".

The object of the invention is to provide a remedy for this.

This takes place according to the invention by a miniaturized microtiter plate which has a body made of plastic and a base made of glass and has 1000 to 4000 vessels (wells), preferably 1400 to 2500 vessels (wells), particularly preferably 1536 vessels (wells), the diameter of the vessels (wells) is approximately 1.0 to 1.8 mm, preferably 1.2 to 1.5 mm, the base of the microtiter plate has a thickness of 0.07 to 0.2 mm, preferably 0.12 to 0.17 mm, particularly preferably 0.15 mm, the distance between the center of the outer vessels (wells) and the edge of the glass base is 4 to 11 mm, preferably ≥ (greater than/equal to) 5.5 mm and the microtiter plate has a lid to prevent evaporation.

The miniaturized microtiter plate usually has a size of 10.0-15.0 x 7.0-10.0 cm, preferably 12.7 x 8.5 cm. However, sizes differing from this are also possible.

The shape of the vessels (wells) is variable. Thus, for example, vessels which are round, have corners or have rounded corners can be used. Round vessels are preferred. It is likewise possible for the number of vessels (wells) to differ from the abovementioned values. The angle between base and wall of the wells can vary between 20° and 90°.

It is important to use the correct material to produce microtiter plates. The body of the microtiter plate consists of plastic such as, for example, polystyrene, polypropylene, polycarbonate, Vectra®, Hostalen®, Topas®. The microtiter plates are usually produced by injection molding (or embossing). The plastic cools after the injection molding. Warping of the microtiter plate is possible during this (because of local differences in the rate of cooling). It is thus beneficial to use a material which produces only a very slight "curvature".

The lid of the microtiter plate is likewise made of plastic and sits form-fittingly on the microtiter plate. The thickness of the base (material: glass) of the microtiter plate (0.07 - 0.20 mm) and the diameter of the vessels (about 1.0 - 1.8 mm), and the distance between the center of the outer vessels (wells) and the edge of the glass base, which is 4 to 11 mm, allow analysis of the microtiter plate using confocal optics. The use of confocal optics has the following advantages:

1. The sensitivity is very high (compared with non-confocal optics) since even individual molecules can be detected in some circumstances (single molecule detection)

2. Because the sensitivity is high, the measurement time can be less and thus the overall rate of analysis of a microtiter plate can be increased (compared with many non-confocal optics) .

3. Since the focus of confocal optics is very small (usually distinctly less than 10 µm), detection of background signals is greatly reduced and thus the signal/noise ratio is better (compared with non-confocal optics).

The base, which consists of glass, of the microtiter plate can be coated with various chemical and biological substances, such as, for example, cellulose, cellulose derivatives, dextrans, polyethylene glycols, in order to suppress nonspecific binding. It ought likewise to be possible for the base to carry biological molecules which specifically bind other substances. The latter is important for use in drug screening, for example for sandwich assays.

Possible embodiments of the microtiter plate according to the invention are described in detail below with reference to Figures 1 to 3. The invention is, however, not restricted to these embodiments.

Fig. 1: Perspective depiction of the microtiter plate with lid lifted off

Fig. 2: Section along plane II-II from Fig. 1

Fig. 3: Section along plane III-III from Fig. 1

Fig. 1 shows a perspective depiction of the microtiter plate with vessels (3). The frame (1) has a length of a = 127 mm and a width of b = 85 mm. The lid (4) with projections (5) is shown in the lifted-off state.

Fig. 2 depicts a section along plane II-II. The glass base (2) is fastened underneath the microtiter plate. The edge distance (a1) is 3 - 8 mm, preferably 6 mm, and the distance (a2) is 6 - 11 mm, preferably 9.5 mm. The corresponding edge distance (b1) in Fig. 3 is likewise 3 - 8 mm, preferably 6 mm, and the distance (b2) is 4 - 11 mm, preferably 6.5 mm. The distances between the center of the outer vessels (wells) and the edge of the glass base (a3, b3) are 4 – 11 mm. The height of the frame of the microtiter plate is (c) = 6 – 20 mm, preferably 6 – 15 mm, particularly preferably 6 mm, and the inner height (c1) is 3 - 12 mm, preferably 3 mm. The vessel diameter (d) is between 1.0 and 1.8 mm, particularly preferably

1.3 mm, the vessel distance (a4) is 2.25 mm and the vessel height (h) is between 2.0 and 7.0 mm.